

Young & Partners and Pharmaceutical Executive Magazine

Executive Summit: Emerging Strategic and Financial Issues in the Pharmaceutical Industry

December 5, 2012
Yale Club in New York City
12:00 Noon to 5:00 P.M.

Co-Sponsored by
Pharmaceutical Executive Magazine and Young & Partners

Agenda

- 12:00 P.M. **Welcoming Comments**
Peter Young, President and Managing Director, *Young & Partners*
William Looney, Editor-in-Chief, *Pharmaceutical Executive*
- 12:10 P.M. **Luncheon and Keynote Speaker**
- The FDA: The Path Going Forward**
Dr. Stephen P. Spielberg, Deputy Commissioner for Medical Products and Tobacco,
The US Food and Drug Administration
- 1:00 P.M. **The Pharmaceutical Industry Strategic and M&A Trends**
Peter Young, President and Managing Director, *Young & Partners*
- 1:30 P.M. **Perspectives on the Future of the Pharma Industry**
Robert J. Hugin, Chairman, Chief Executive Officer, President,
Celgene Corporation
- 2:10 P.M. **The Pharmaceutical Market: Trends, Issues and Outlook**
Doug Long, Vice President, *IMS Health Inc.*
- 2:50 P.M. **The Increasing Clout of Personalized Medicine**
William D. Baird, Chief Financial Officer, *Amicus Therapeutics*
Glenn A. Miller PhD, VP and Head of Personalized Healthcare and
Biomarkers Strategy, Portfolio and Alliances, *AstraZeneca Pharmaceuticals*
- 3:30 P.M. **Biotech Deal Making – M&A, Licensing and Partnering Trends**
Randolph Guggenheimer III, Managing Director, *Young & Partners*
- 4:00 P.M. **Speaker Roundtable**
Moderator: Peter Young, President, *Young & Partners*
Participants: Executive Summit Speakers
- 5:00 P.M. **Concluding Comments**

The FDA: The Path Going Forward

DR. STEPHEN P. SPIELBERG

**DEPUTY COMMISSIONER FOR MEDICAL PRODUCTS AND TOBACCO,
THE US FOOD AND DRUG ADMINISTRATION**

We are in the middle of a biological revolution. This is a difficult situation for society in that our science is evolving much more quickly than our sociology as a species. Change is being driven today by disruptive technologies, fundamental modifications to our understanding of human biology, and radical changes in the diagnosis and treatment of disease. Much of this change is occurring at a molecular and genomic level. We have moved rapidly from discovering individual genes to whole genome associations and next generation whole genome sequencing.



For a historical perspective on the revolutionary scientific discoveries of recent decades, it is helpful to remember a 1981 New England Journal of Medicine report on the discovery of a new immune deficiency disease: HIV. If the onset of the HIV/AIDS epidemic had occurred just 20 years earlier in 1961, the medical community would not have had the appropriate knowledge to even discuss treatment or prevention of the disease, let alone develop the drugs needed to do such things. In 1961 we didn't know what retroviruses were, and thus this disease would have been akin to the black plague of Europe from many centuries ago. Just 20 years in the evolution of medicine and science provided enough knowledge to understand the etiology or basis of the disease and therefore discussion about how to treat and hopefully prevent it could begin.

Today, as this biological revolution takes shape, we are in the midst of a reclassification of medicine. Diagnoses and diseases today are classified based on etiology and pathogenesis as opposed to the names of those who discovered them. With regard to cancer, we are no longer talking about classifying diseases based on cell or tissue of origin, but on the molecular drivers of the oncologic process.

These breakthroughs in science and thinking about medicine have allowed for the entrance of a new field which has existed for years but only recently has gained serious traction: Personalized Medicine. This is the type of medical care doctors and patients have always wanted. It is about treating the individual as opposed to a population with a similar symptom or ailment. Doctors can now discuss treatments with patients and how those treatments will affect them individually instead of simply giving patients population based odds of success when utilizing a particular treatment.

One particular disease which is being treated more and more utilizing a personalized medicine approach is Cystic Fibrosis (CF). This is due in large part to the work of a patient advocacy group: The Cystic Fibrosis Foundation. This group raised money in order to help fund the cloning of the particular affected gene, the discovering of the mechanisms which cause the disease, and developed the clinical trial network necessary to test treatment options. We now know what causes CF. It is a series of mutations within a particular gene. There is one dominant mutation; however there are several others which also affect the gene. The CF foundation, partnering with Basic Sciences and with a drug developer sponsor, took on the creation of a drug for one of these other mutations, which affects only about 1200 CF patients. This work led to the discovery and development of a drug which has been approved to treat patients within this subset of CF.

This drug moved from Investigatory New Drug (IND) status to approval within 6 years vs. the usual 12-14 years for many drugs. The FDA review time was three months, exactly half of the expedited priority review period. This was possible because 95% of patients involved in the clinical trial benefited from the drug and the effect size was enormous. This is an astounding example of personalized medicine within a rare disease

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space and a perfect example of how innovation in drug development and early and frequent communication between industry and the FDA has made a more timely development and review process possible. This has led to more drugs being approved by the FDA, more quickly.

While clinical trials and the FDA review are becoming more efficient, and the emergence of personalized medicine provides many exciting opportunities, there are fresh challenges facing drug developers in this new era of medicine. With many diseases there are very complex interactions between different and/or multiple genes and environmental variables which must be considered. In addition there is significant complexity that goes along with the development of a drug and companion diagnostic combination with regard to regulation. The drug and diagnostic may be developed by separate companies within different countries which can create a host of issues. For example, in Europe diagnostics are not regulated by the EMA, but on a country by country basis.

With regard to the paradigm shift in medicine towards a more personalized approach, those companies focused on combination drug and companion diagnostics may soon find themselves having to restructure or refocus their efforts. As personalized medicine evolves along with our understanding of the human genome, we may someday reach a point where companion diagnostics are no longer necessary. We will be able to determine whether or not a patient should respond to a particular drug simply by studying the patient's available genome sequence. In addition we will see more of a shift from the block-buster drug model to the model of several mini-buster drugs which may require changes in company structure related to manufacturing, post-market data collection, etc.

The FDA understands these challenges and has realigned itself in order to better coordinate across its different divisions. Certain treatments are much more complex and cut across the different divisions including drugs, diagnostics, cell therapy, etc. Despite the challenges noted, I am optimistic that as a result of innovations in drug discovery and development and through collaboration between all industry stakeholders, the industry will be successful in treating diseases such as cancer far more effectively.

The Current and Future State of the Pharmaceutical Industry

PETER YOUNG
PRESIDENT, YOUNG & PARTNERS

This is both an exciting and challenging time for the pharma industry and its sister industry, biotech. There are both positive and negative developments affecting the pharma industry.

On the positive front, aging populations in the developed countries favor growth in healthcare and pharmaceutical demand, there is strong growth in demand in Asia from economic strength and population size, new technologies have been developed to accelerate drug discovery and development, there are some signs that drug discovery success rates are improving, lifestyle and aging related drug therapies are showing tremendous growth potential relative to other drug markets, personalized medicine and stem cell related solutions have become a reality, substantial efforts by the FDA to streamline drug approvals has had a positive effect overall, and the 2010 U.S. Health Care Reform bill that was passed has the potential to increase the number of patients covered for prescription drugs.



On the negative front, the business model of the large ethical drug companies is clearly broken, the R&D costs required to launch new drugs are now extremely high (about \$1.1 billion per drug) and continue to escalate (even as the industry adopts new techniques to increase the productivity of R&D), it is now taking an average of over 12 years to bring a new drug to market, there are a variety of threats to ethical drugs outside the West - with lower pricing and weaker patent protection, and drug safety issues are plaguing many already established drugs, patents continue to expire in large numbers, and new competitors are emerging from India and China who are aspiring to evolve from generics and API production to being fully integrated pharmaceutical and biotech companies.

In addition, the replacement of the historic business model of the pharma industry has been difficult for companies. Both big and small pharmaceutical companies have been revamping and adjusting their strategies to survive in this new business environment.

Current strategies range from diversification, large scale mergers, exiting the pharma industry, geographic expansion, regional consolidation, pursuit of biologics, expansion of generics, movement into vaccines, pursuit of orphan and niche drugs, etc. Virtually all pharma companies are pursuing biotech acquisitions and partnering/alliances.

However, no clear picture has emerged with regard to who the winners and losers will be.

In terms of M&A, in the first three quarters of 2012, 26 deals were completed worth \$19.2 billion versus 49 deals completed worth \$65.6 billion during all of 2011. This represents a major slowdown in activity. This is separate from biotech acquisitions, licensing and partnering.

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Although there were no mega deals, there were five deals with over \$1 billion in equity value: Couckinvest NV's acquisition of Omega Pharma NV, Sandoz's acquisition of Fougera, TPG Capital's acquisition of Par Pharmaceutical, GlaxoSmithKline's acquisition of Human Genome Sciences, and Bristol Myers Squibb's acquisition of Amylin Pharmaceutical.

As of September 30, 2012, the value of the deals announced but not closed was a modest \$12.6 billion (12 deals), the largest of which is Watson's pending acquisition of Actavis.

Finally, what is the future outlook like for the pharma industry?

The business outlook for pharma companies is mixed, as pharma companies struggle to realign themselves to a new business model that will work. The solution will be different for each company. However, the biggest challenge is on the shoulders of the big pharma companies whose structural underpinnings have been undermined the most. There are recent signs that Big Pharma is beginning to downsize as the patent expirations get closer or have arrived.

Generics are being challenged now that the peak of patent expirations have passed and they are forced to either merge or move into more specialized areas.

The stock market will continue to penalize the ethical pharma industry as long as the structural changes are working their way through the industry and solutions are being implemented.

Young & Partners expects M&A activity to be modest in the near-term for a number of reasons, including the major uncertainties around the global economic and financial picture. The effect will be greatest on the large deals.

However, we expect volume to pick-up as pharma companies merge or acquire to achieve scale and enhance their product pipelines. M&A activity in emerging markets will grow as companies look to these markets for growth.

The need to fill the shrinking drug pipeline will continue to fuel mergers and acquisitions, in-licensing arrangements, and the formation of partnerships and joint ventures.

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Perspectives on the Future of the Pharma Industry

ROBERT J. HUGIN
CHIEF EXECUTIVE OFFICER, PRESIDENT,
CELGENE CORPORATION

It is an exciting time to be in the pharmaceutical industry. There have been numerous major medical and scientific advances in recent years. These advances have led to a higher quality of life and extended the lifespan for millions of patients. One major medical innovation, the sequencing of the human genome, has advanced even more rapidly than Moore's Law would predict. As of 2011 there were in excess of 3,000 medicines in development. This includes 932 medicines for cancer and 460 for rare diseases.



Along with these recent advances in science and medicine, there are numerous reasons to be optimistic about the future of the pharmaceutical industry. The primary reason is the pharmaceutical industry's proven track record of success in making a difference in patients' lives. Examples of this success include a 90% reduction in AIDS and the consequences of AIDS through the use of therapeutics, a 45% reduction in deaths due to heart attack and heart failure over the period from 1999 to 2005, declining cancer death rates, and a lower rate of nursing home care amongst those Alzheimer's patients who undergo therapeutic treatment vs. those who do not.

Going forward pharmaceutical industry growth will be increasingly driven by emerging markets and a shift in population demographics. Emerging markets have growing middle class populations with increasing economic significance. These societies will soon be seeking more and better healthcare and this will create robust demand for branded generic drugs. This is particularly important for large pharmaceutical companies because they have the size and scale to take advantage of the opportunities within those markets in a timely fashion. The rapid increase in the number of patients over the age of 60 as a percentage of the total population will also contribute significantly to demand for pharmaceuticals over the next several decades.

A vibrant pharmaceutical industry is important for the US economy because it is an industry which creates many good, high-paying jobs. There are more than 650,000 jobs in the US biopharmaceutical sector. Each of these direct biopharmaceutical jobs supports an average of five additional jobs in other sectors.

The pharmaceutical industry does though face some challenges going forward. One challenge is the unsustainable upward trend in US healthcare costs. Drug development costs are increasing. The average costs to develop one new approved therapy - including the cost of failures - increased approximately 50% between the late 1990s and early 2000s to \$1.2 Billion, and today only 2 in 10 medicines approved for use have revenues which exceed their average R&D production costs. One additional hurdle for drug developers going forward is the uncertainty of intellectual property protection which is so vital to innovation within the industry.

Overall there are enormous opportunities in the pharmaceutical industry. There are many stakeholders and if they are able to work together to foster innovation and growth, great strides will be made for patients and the US economy.

The Pharmaceutical Market: Trends, Issues, and Outlook

DOUG LONG
VICE PRESIDENT, IMS HEALTH

Worldwide healthcare costs are on an unsustainable upward trajectory. Healthcare costs are projected to increase going forward in line with increased human life expectancy. In most major developed countries drug costs account for only a small amount of the total healthcare budget. Drug costs within the United States, for example, account for only about 12% of healthcare costs. Yet governments are attempting to lower pharmaceutical costs through changing the product mix available, including the utilization of generic drugs, and reducing prices.



IMS projects that between now and 2016 mature markets will face low growth and more cost containment. The European pharmaceutical market, in particular, will be under pressure with severe hospital debt and historically low growth. Pharming markets will have high growth but with mixed fortunes for drug originators.

The global pharmaceutical industry's cumulative aggregate growth is expected to be 3-6%, with a value of over \$1.1 trillion through 2016. Original brands growth will slow and their share will decline as generic drugs garner more and more market share. Generics have grown at twice the rate of the global pharmaceutical market.

With regard to the US pharmaceutical industry, growth has moderated as a result of increased cost sharing for consumers in the form of higher prescription drug deductibles, the economic downturn, and an innovation drought in recent years. In addition there have been safety concerns over various drugs, prescription to over-the-counter conversions, and lost sales in name brands due to the ongoing introduction of first time generic drugs. Due to patent expirations, a number of the classes of drugs which have enjoyed high sales historically will see revenues decline in coming years. As a result, the US pharmaceutical industry is projected to grow at a rate of 0-3%. However, although 2012 drug launches aren't projected to be blockbusters, 2010/11 launches have shown promise thus far, hoping to reverse a dramatic decline in blockbuster level drug launches from 2007 to 2009. This could provide a much needed boost to the relatively stagnant market.

IMS believes one of the bright spots in the US pharmaceutical industry is biosimilars. These drugs are expected to succeed because payers will increasingly see biologics as their main cost driver due to the decline in savings from small molecule generics after 2015. IMS believes that the US will represent the cornerstone of the biosimilars market over the long run, with the potential for up to \$25 Billion in sales by 2020. In addition, historically, in the US, there has been relatively low patient adherence/compliance with prescription drugs and increased adherence could lead to significant savings for the overall healthcare system. We see this as a major opportunity for positive progression of the industry as a whole.

The Increasing Clout of Personalized Medicine

WILLIAM D. BAIRD
CHIEF FINANCIAL OFFICER, AMICUS THERAPEUTICS

Personalized medicine is focused on therapies utilizing medicine with a proven molecular marker and often with a companion diagnostic. These medicines can be widely used such as Herceptin, which had sales of about \$5.7 Billion in 2011, or treat rare orphan diseases.



Orphan drugs are a niche market within the broader market of personalized medicine. Orphan drugs are those developed to treat patient populations of fewer than 200,000 patients. According to NORD there are about 6,800 diseases which qualify as orphan diseases. Together these diseases affect about 25 million Americans, or about 10% of our nation's population. Within orphan products, there is a subset of drugs which can be described as ultra-orphan products and which some characterize as products which treat patient populations of fewer than 10,000. Some examples of personalized ultra-orphan products, or ultra-orphan products which target a genetic subset, include Vertex's Kalydeco, Sarepta's Eteplirsen, Amicus' Migalastat, and PTC Therapeutics' Ataluren.

Kalydeco is a small molecule targeting the G551D mutation which affects about 4% of Cystic Fibrosis patients. On February 23, 2011 Vertex announced top-line Phase 3 data on Kalydeco. The drug showed a highly significant improvement relative to placebo. Secondary endpoints and the drug's safety profile were also positive for Kalydeco. The drug was subsequently approved by the FDA in fewer than six months. Vertex experienced a \$1.7 Billion increase in market cap as investors reacted to Kalydeco's Phase 3 results.

Sarepta's Eteplirsen is an exon-skipping approach to treating exon-51 of the dystrophin gene. Approximately 13% of Duchenne Muscular Dystrophy patients may have mutations amenable to this exon-skipping method of therapy. In July 2012, Sarepta announced 36-week data from a 12-patient Phase 2 study showing patient improvement. In October 2012, Sarepta released supportive 48 week data from the same study. Sarepta's stock price rose by 146% on release of 36-week data, and by 200% on 48-week data.

Amicus' Migalastat is a next generation therapy for Fabry disease. This therapy is meant to treat a subset of patients with Fabry disease. The drug is a small molecule chaperone which binds itself to the affected enzyme and helps it move to the lysosome where it can have a positive effect. Amicus' Migalastat has attracted the interest of GlaxoSmithKline and Amicus has partnered with GSK to develop the drug.

PTC's Ataluren is a small-molecule designed to read-through nonsense mutations. Nonsense mutations are a common genetic mutation observed in hundreds of orphan diseases. Clinical trials are currently testing the effectiveness of Ataluren in treating Duchenne and Cystic Fibrosis. In July 2008, Genzyme paid \$100M upfront for ex-US commercial rights to the Ataluren program.

Clearly there is a lot of interest and a lot of clout wielded by companies in the orphan disease space. Keeping this clout is going to be a challenge for orphan drug developers due to threats to drug cost reimbursement. However it is likely that with the paradigm shift into personalized medicine, and the cost savings which have been shown to come as a result of therapies such as these, it is inevitable that this industry will remain influential. Remaining influential or retaining this clout in the pharmaceutical industry will require reinvestment of funds gained from successful drug launches in order to treat even more patients in the rare disease space.

The Increasing Clout of Personalized Medicine

GLENN A. MILLER, PH.D.

**VICE PRESIDENT AND HEAD OF STRATEGY, PORTFOLIO, AND ALLIANCES FOR
PERSONALIZED HEALTHCARE AND BIOMARKERS
ASTRAZENECA PHARMACEUTICALS**

Personalized medicine is important to developers, payers, prescribers, and patients, and is ultimately the right thing to do. Personalized medicine is important to the various players within the medical and pharmaceutical industries for different reasons. To the pharmaceutical industry or drug developers it means an approved therapeutic and possibly an approved companion diagnostic. To payers it means managing individual patients, and individual patients' spend or costs. It means knowing what, when and why they are paying. To doctors and/or prescribers personalized medicine really means nothing. They are practicing personalized medicine every day. They will, however, benefit from this paradigm shift in that they need higher quality information, regardless of its source, and better drugs which allow them to more effectively treat their individual patients. Finally, personalized medicine for patients ultimately means better outcomes, and feeling better.



Some of the frequently referred to problems with personalized medicine today include the length of time to market for an effective drug in the space, the high expense of R&D in order to create these drugs, and the fact that the approach isn't always successful. One response to these notions at AstraZeneca has been to look at success rates of drug development programs utilizing a personalized vs. a non-personalized health care approach. Within the programs we studied, we noted that the attrition rate of those without a personalized health care approach was close to 60%. Programs which were exploring a personalized health care approach had attrition rates of less than 40% and those programs which had a companion diagnostic which was being developed along with the drug had even lower attrition. Therefore at AstraZeneca there has been a push to integrate personalized health care throughout the drug discovery and development process.

We at AstraZeneca now, for all Lead Optimization (LO) programs, have a Research Use Only (RUO) biomarker associated with them. This initiative may or may not be successful, but this is happening for all LOs. We designate a discovery project team, with the expertise and internal and external lab facilities to convert RUO biomarkers to Investigational Use Only (IUO) biomarkers for use in first clinical studies, within each therapeutic area. From there we utilize our own skills as well as partnerships and relationships external to AstraZeneca to convert the IUO into an in vitro diagnostic (IVD) product. The goal of the program is to develop a regulatory approved and ultimately marketable product, including the IVD.

More than three quarters of our drug candidates today have patient stratification as a key part of their development strategy. In addition most of our drugs approaching Phase 3 clinical trials have a companion diagnostic planned or already in active development. We have a drug on the market today in IRESSA, which was developed this way. These actions are proof of the increasing clout of personalized medicine.

What is the future of personalized medicine? One major area related to personalized medicine which we see and expect will continue evolving rather significantly is precompetitive alliances between companies and academia. We believe these alliances will allow for streamlining and prevention of repetitiveness in clinical testing for pharmaceutical products. This will greatly benefit all players within the medical community because drugs can be developed and tested more quickly and more efficiently.

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Biotech Deal Making: M&A, Licensing, and Partnering Trends

RANDY GUGGENHEIMER III
MANAGING DIRECTOR, YOUNG & PARTNERS

The biotech industry is growing because of a number of positive trends, including demographics and technological advances. A number of biotech companies have built successful, substantial enterprises. The outlook is positive because of continuing innovation and the relative lack of generic competition for biologics. Pharmaceutical companies need new products and product candidates to replace products whose patents are expiring. This has led to strong stock market performance of biotech companies and slightly better access to equity capital in the public markets. On the negative side, financing for clinical stage companies has been difficult to come by from venture capital companies as development times and costs have expanded. In addition, the relatively low number of IPOs has limited that exit strategy.



Financing activity has been somewhat higher in the first 9 months of 2012 vs. 2011 and stock price performance for biotechs has been very strong. This is due to increased M&A activity, new product approvals and positive clinical data.

M&A activity in the first three quarters of 2012 has been at record levels, with \$19 billion of deals completed. This has been driven by large deals, including two Hepatitis C (HCV) company acquisitions totaling \$13 billion (Pharmasset and Inhibitex).

The Gilead/Pharmasset transaction was valued at about \$11 billion (an 89% premium) and was driven by Gilead's desire for 7977, a HCV product in Phase 3. Gilead has benefited substantially from the acquisition as its stock price has doubled since the time of the acquisition, primarily based on positive data from 7977.

The Bristol-Myers Squibb/Inhibitex deal was valued at about \$2.5 billion (a 163% premium) and was driven by BMS's desire for 189, a HCV product in Phase 2. BMS's stock declined by over 10% several months after the acquisition when it halted the trial of 189 due to serious safety issues and subsequently discontinued development of the product.

The AstraZeneca/Ardea deal was valued at \$1.3 billion (a 54% premium) and was driven by AZ's desire for lesinurad, a gout product in Phase 3 to help offset several patent expirations. AZ continues to develop lesinurad and its stock price has been affected by the retirement of its CEO rather than lesinurad developments.

Earnout transactions became very popular in the 2009-2011 periods, growing as high as 67% of biotech M&A transactions in 2010. In the first three quarters of 2012, earnout deals accounted for 29% of transactions as there was significant competition for deals, including the HCV deals, and the equity markets improved.

Biotech product licensing continues to be significant. Although the number of deals has fallen somewhat over the last couple of years the "BioWorld dollars" has increased, reflecting the level of competition and need for attractive products among pharmaceutical and large biotech companies.